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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/683,549	10/10/2003	Fabian Somers	DI-5954 (BXTD 9004.6)	2624

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SENNIGER POWERS LEAVITT AND ROEDEL
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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/683,549	SOMERS ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 19-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040126*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant's election without traverse of the species erythropoietin plus Gly-His in the reply filed on February 4, 2005 is acknowledged.

Claim 18 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on February 4, 2005.

2. Claims 19 and 20 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Dependent claims 19 and 20 recite that the peptide stabilizers can be derivatives of various dipeptides or tripeptides. However, independent claim 16, upon which claims 19 and 20 depend, does not recite that the peptide stabilizer can be a derivative of a dipeptide or tripeptide.

3. Applicant is advised that should claims 1, 16, or 34 be found allowable, then claims 9, 23, and 36, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 1 and 9; claims 16 and 23; and claims 34 and 36; are identical in scope. Because the independent claims exclude serum albumin from the claimed compositions, then necessarily human serum albumin will be absent from the claimed compositions.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

5. Claims 1-4, 9-17, 19, 21-26, 30-34, and 36 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Sato et al (U.S. Patent Application Publication 2003/0092622). Sato et al teach stabilized pharmaceutical compositions comprising a protein such as erythropoietin which is produced recombinantly in BHK or CHO cells and a stabilizer which is Trp or a derivative thereof in a concentration of 0.1-300 mM, preferably 1-10 mM. The EPO concentrations can range preferably from 750 to 72,000 IU/ml. The derivatives can be dipeptides such as Cbz-Gly-Trp, Cbz-Gly-Trp-OMe, Cbz-Gly-Gly-Trp-OMe, Gly-Trp, Ala-Trp, etc. The compositions are free of protein stabilizers such as human serum albumin. The compositions can comprise a surfactant such as polysorbate 20 or 80. Surfactant concentrations are preferably 0.005-3% (w/v). See, e.g., paragraphs [0042], [0043], [0046]-[0048], [0056], and [0057]. With respect to instant claims 1, 19, and 34, the Trp derivatives of Sato et al are deemed to constitute "derivatives" of the specific peptide stabilizers claimed by Applicants, because of their similarity in structure (i.e. dipeptides or tripeptides having at least one amino acid in common) and structure (i.e. ability to stabilize protein compositions).

6. Claims 3-7, 24-29, and 35 are rejected under 35 U.S.C. 103(a) as being obvious over Sato et al (U.S. Patent Application Publication 2003/0092622) as applied against claims 1-4, 9-17, 19, 21-26, 30-34, and 36 above, and further in view of the WO Patent Application 02/14356. Sato et al are not limited to stabilizing any particular type of erythropoietin, but do not teach stabilizing an erythropoietin which is erythropoietin omega. The WO Patent Application '356 teaches erythropoietin omega to be a form of erythropoietin which is useful in treating fatigue, pain, chronic heart failure, dysrythmia and dementia. See, e.g., the Abstract; page 4, line 24 - page 9, line 14; and claim 1. It would have been obvious to one of ordinary skill in the art at the time

Applicants' invention was made to stabilize the erythropoietin omega of the WO Patent Application '356 using the stabilizing agents of Sato et al because it would be desirable to stabilize the erythropoietin omega of the WO Patent Application '356 so as to preserve its therapeutic activities, and because the stabilizing agents of Sato et al have been used to preserve very closely related erythropoietin analogs and therefore would have been expected to be useful in stabilizing erythropoietin omega.

7. Claims 1 and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Cormier et al (U.S. Patent Application Publication 2002/0058608). Cormier et al disclose an aqueous composition comprising a drug which is preferably a protein or a polypeptide and a buffer which is preferably Gly-His, at least partly in salt form. The drug can be erythropoietin. The buffer is present in a concentration of 10 mM to 1 M (2.1-212 g/L), preferably 25-250 mM (5.3-53 g/L). No serum albumin is present in the composition. See, e.g., paragraphs [0034], [0041], [0047] and claims 1, 6, and 8.

8. Claims 2-4, 11, 16, 17, and 19-24 are rejected under 35 U.S.C. 103(a) as being obvious over Cormier et al (U.S. Patent Application Publication 2002/0058608). Application of Cormier et al is the same as in the above rejection of claims 1 and 8-10. Cormier et al do not specifically teach a composition comprising both erythropoietin and Gly-His, and do not teach the buffer concentration of instant claims 11 and 22. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer erythropoietin using the Gly-His buffer of Cormier et al because Cormier et al disclose that erythropoietin is a protein which can usefully be administered in their formulations, and because Gly-His is a preferred buffer for Cormier et al's compositions. With respect to the limitation "recombinant" in instant claims 3

and 24, process of making limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal buffer concentrations embraced by the disclosure of Cormier et al because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

9. Claims 3-7 and 24-29 are rejected under 35 U.S.C. 103(a) as being obvious over Cormier et al (U.S. Patent Application Publication 2002/0058608) as applied against claims 2-4, 11, 16, 17, and 19-24 above, and further in view of the WO Patent Application 02/14356. Cormier et al are not limited to stabilizing any particular type of erythropoietin, but do not teach stabilizing an erythropoietin which is erythropoietin omega. The WO Patent Application '356 teaches erythropoietin omega to be a form of erythropoietin which is useful in treating fatigue, pain, chronic heart failure, dysrythmia and dementia. See, e.g., the Abstract; page 4, line 24 - page 9, line 14; and claim 1. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to formulate the erythropoietin omega of the WO Patent Application '356 in the compositions of Cormier et al because it would be desirable to administer the erythropoietin omega of the WO Patent Application '356 iontophoretically, and because the compositions of Cormier et al have been used to administer a wide range of proteins and therefore would have been expected to be useful in administering erythropoietin omega. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations for the erythropoietin omega to be administered in the compositions of Cormier et al as modified above by the WO

Patent Application '356 because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

10. Claims 12-15 are rejected under 35 U.S.C. 103(a) as being obvious over Cormier et al (U.S. Patent Application Publication 2002/0058608) as applied against claims 1 and 8-10 above, and further in view of Holladay et al (U.S. Patent No. 6,328,728). The compositions of Cormier et al are to be administered by transdermal electrotransport, i.e. iontophoretically (see, e.g., the Abstract, paragraph [0003], and claim 1), but Cormier et al do not teach the presence of a surface active agent in the composition comprising the protein or polypeptide. Holladay et al et al teach including a surfactant such as a polyoxyalkylene sorbitan fatty acid ester in a composition comprising a protein or polypeptide which is to be electrotransported across a body surface, i.e. across the skin. The surfactant has the benefit of increasing the flux of the protein or polypeptide across the body surface and of decreasing the biodegradation of the proteins or polypeptides. See, e.g., column 3, line 55 - column 4, line 6, and claims 4 and 8. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to include a surfactant such as a polyoxyalkylene sorbitan fatty acid ester of Holladay et al in the compositions of Cormier et al so as to increase the flux and to decrease of biodegradation of the proteins or polypeptides to be administered by Cormier et al. Note that motivation to combine under 35 U.S.C. 103 need not be the same as Applicants' expressed motivation. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations for the surfactants in the compositions of Cormier et al as modified above by Holladay et al because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

11. Claims 30-34 and 36 are rejected under 35 U.S.C. 103(a) as being obvious over Cormier et al (U.S. Patent Application Publication 2002/0058608) as applied against claims 2-4, 11, 16, 17, and 19-24 above, and further in view of Holladay et al (U.S. Patent No. 6,328,728). The compositions of Cormier et al are to be administered by transdermal electrotransport, i.e. iontophoretically (see, e.g., the Abstract, paragraph [0003], and claim 1), but Cormier et al do not teach the presence of a surface active agent in the composition comprising the protein or polypeptide. Holladay et al et al teach including a surfactant such as a polyoxyalkylene sorbitan fatty acid ester in a composition comprising a protein or polypeptide which is to be electrotransported across a body surface, i.e. across the skin. The surfactants have the benefit of increasing the flux of the protein or polypeptide across the body surface and of decreasing the biodegradation of the proteins or polypeptides. See, e.g., column 3, line 55 - column 4, line 6, and claims 4 and 8. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to include a surfactant such as a polyoxyalkylene sorbitan fatty acid ester of Holladay et al in the compositions of Cormier et al so as to increase the flux and to decrease of biodegradation of the erythropoietin to be administered by Cormier et al. Note that motivation to combine under 35 U.S.C. 103 need not be the same as Applicants' expressed motivation. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations for the surfactants in the compositions of Cormier et al as modified above by Holladay et al because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

12. Claim 35 is rejected under 35 U.S.C. 103(a) as being obvious over Cormier et al (U.S. Patent Application Publication 2002/0058608) in view of the WO Patent Application 02/14356 as applied against claims 3-7 and 24-29 above, and further in view of Holladay et al (U.S. Patent No. 6,328,728). The compositions of Cormier et al as modified above by the WO Patent Application '356 are to be administered by transdermal electrotransport, i.e. iontophoretically (see, e.g., the Abstract, paragraph [0003], and claim 1), but Cormier et al do not teach the presence of a surface active agent in the composition comprising the protein or polypeptide. Holladay et al et al teach including a surfactant such as a polyoxyalkylene sorbitan fatty acid ester in a composition comprising a protein or polypeptide which is to be electrotransported across a body surface, i.e. across the skin. The surfactants have the benefit of increasing the flux of the protein or polypeptide across the body surface and of decreasing the biodegradation of the proteins or polypeptides. See, e.g., column 3, line 55 - column 4, line 6, and claims 4 and 8. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to include a surfactant such as a polyoxyalkylene sorbitan fatty acid ester of Holladay et al in the compositions of Cormier et al as modified above by the WO Patent Application '356 so as to increase the flux and to decrease of biodegradation of the erythropoietin omega to be administered. Note that motivation to combine under 35 U.S.C. 103 need not be the same as Applicants' expressed motivation. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations for the surfactants in the compositions of Cormier et al as modified above by the WO Patent Application '356 and Holladay et al because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

13. Claims 1 and 9-15 are rejected under 35 U.S.C. 103(a) as being obvious over Bjorn et al (U.S. Patent Application Publication 2003/0162711). Bjorn et al teach compositions comprising growth hormone, an amino acid which can be a derivative of histidine such as Gly-His, and a surfactant such as polysorbate. The compositions do not contain serum albumin. See, e.g., the Abstract; paragraph [0070]; and claims 4 and 8. Bjorn et al do not teach the specific combination of growth hormone, Gly-His, and polysorbate. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form compositions according to Bjorn et al comprising growth hormone, Gly-His, and polysorbate, because Bjorn et al specifically name Gly-His and polysorbate as being useful in forming stabilized growth hormone-containing compositions, and because the resulting compositions have only the increased stability which would have been expected in view of Bjorn et al. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations for the components present in the compositions of Bjorn et al because concentration is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts.

14. Wan et al (U.S. Patent Application Publication 2004/0166572 - see, e.g., paragraphs [0022] and [0024]) cited as art of interest, being essentially duplicative of the references applied above. The WO Patent Application 2001/60420 (see, e.g., claims 3 and 5), Shirley et al (U.S. Patent No. 6,306,402 - see, e.g., claims 1 and 3), and Ron et al (U.S. Patent No. 5,597,897 - see, e.g., Example 3 and Table 4) are cited as art of interest, especially with respect to non-elected proteins and peptide stabilizers.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

March 25, 2005